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60/149,395 17 August 1999 (17.08.1999) US

[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE TREATMENT OF TUMOR

MTVIRFFPAASATKRVLPVLRVSSPRTWNPVSPRIAPRLPKRMSGAPTAGAALMLCAATAVLLSAQGGPV
QSKSPRFASWDEMNVLAHGLLQGLREHAERTRSQLSALERRLSACGSACQTEGSTDLPLAPESRVDPEVLH
SLQTLKAQNSRIQQLFHKVAQQORHLEKQLRIQHLQSQFGLLDHKKHLDHEVAKPARRKRLPEMAQVPDPAHNV
SRLHRLPRDCQELFQVGERQSGLFELIQPGSSPFLVNCMTSDGGWTVIQRHDGSDVDFNRPWEAYKAGFGDPHG
EFWLGLEKVHSITGDRNSRLAVQLRDWDGNAELLQFSVHLGGEDTAYSLQLTAPVAGQLGATTVPVPSGLSVFPST
WDQDHDRLRRDKNCAKSLSGGWVFGTCSHNSLNGQYFRSIPQQRQKLKKGIFWKTWRGRYYPLOATTMLIQPMAAEAS

Transmembrane domain: Amino acids 51-70
N-glycosylation site: Amino acids 224-228
cAMP- and cGMP-dependent protein kinase phosphorylation sites:
Amino acids 46-50;118-122
N-myristoylation sites: Amino acids 50-56;129-135;341-347;
357-363
Fibrinogen beta and gamma chains C-terminal domain signature:
Amino acids 396-409

(57) Abstract: The invention concerns compositions and methods for the diagnosis and treatment of neoplastic cell growth and proliferation in mammals, including humans. The invention is based upon the identification of genes that are amplified in the genome of tumor cells. Such gene amplification is expected to be associated with the overexpression of the gene product as compared to normal cells of the same tissue type and contribute to tumorigenesis. Accordingly, the proteins encoded by the amplified genes are believed to be useful targets for the diagnosis and/or treatment (including prevention) of certain cancers, and may act as predictors of the prognosis of tumor treatment. The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

of Washington, Seattle, Washington). One or more of the ESTs used in the assembly was derived from a library constructed from tissue obtained from the parotid (salivary) gland of a human with parotid cancer. The consensus sequence obtained therefrom is herein designated as DNA56019.

In light of an observed sequence homology between the DNA56019 sequence and Incyte EST clone no. 1327836, Incyte EST clone no. 1327836 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 27 (SEQ ID NO:27) and is herein designated as DNA64884-1527.

The entire coding sequence of DNA64884-1527 is included in Figure 27 (SEQ ID NO:27). Clone DNA64884-1527 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 79-81 and ending at the stop codon at nucleotide positions 391-393 (Figure 27). The predicted polypeptide precursor is 104 amino acids long (Figure 28; SEQ ID NO:28). The full-length PRO1245 protein shown in Figure 28 has an estimated molecular weight of about 10,100 daltons and a pI of about 8.76. Analysis of the full-length PRO1245 sequence shown in Figure 28 (SEQ ID NO:28) evidences the presence of a variety of important polypeptide domains, wherein the locations given for those important polypeptide domains are approximate as described above. Analysis of the full-length PRO1245 sequence shown in Figure 28 evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 18; N-myristoylation sites from about amino acid 8 to about amino acid 14, from about amino acid 65 to about amino acid 71, from about amino acid 74 to about amino acid 80, and from about amino acid 88 to about amino acid 94; and a prokaryotic membrane lipoprotein lipid attachment site from about amino acid 5 to about amino acid 16. Clone DNA64884-1527 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203155.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 28 (SEQ ID NO:28), evidenced some homology between the PRO1245 amino acid sequence and the following Dayhoff sequences: SYA_THETH, GEN11167, MTV044_4, AB011151_1, RLAJ2750_3, SNELIPTRA_1, S63624, C28391, A37907, and S14064.

EXAMPLE 17

Isolation of cDNA Clones Encoding Human PRO1759

DNA76531-1701 was identified by applying the proprietary signal sequence finding algorithm described in Example 2 above. Use of the above described signal sequence algorithm allowed identification of an EST cluster sequence from the LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, CA, designated DNA10571. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul *et al.*, Methods in Enzymology, 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs used in the assembly was derived from pooled eosinophils of allergic asthmatic patients. The consensus sequence obtained therefrom is herein designated as DNA57313.

In light of an observed sequence homology between the DNA57313 sequence and Incyte EST 2434255,

the clone including this Incyte EST 2434255 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 29 (SEQ ID NO:29) and is herein designated as DNA76531-1701.

The entire coding sequence of DNA76531-1701 is included in Figure 29 (SEQ ID NO:29). Clone DNA76531-1701 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 125-127 and ending at the stop codon at nucleotide positions 1475-1477 (Figure 29). The predicted polypeptide precursor is 450 amino acids long (Figure 30; SEQ ID NO:30). The full-length PRO1759 protein shown in Figure 30 has an estimated molecular weight of about 49,765 daltons and a pI of about 8.14. Analysis of the full-length PRO1759 sequence shown in Figure 30 (SEQ ID NO:30) evidences the presence of a variety of important polypeptide domains, wherein the locations given for those important polypeptide domains are approximate as described above. Analysis of the full-length PRO1759 sequence shown in Figure 30 evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 18; transmembrane domains from about amino acid 41 to about amino acid 55, from about amino acid 75 to about amino acid 94, from about amino acid 127 to about amino acid 143, from about amino acid 191 to about amino acid 213, from about amino acid 249 to about amino acid 270, from about amino acid 278 to about amino acid 299, from about amino acid 314 to about amino acid 330, from about amino acid 343 to about amino acid 359, from about amino acid 379 to about amino acid 394, and from about amino acid 410 to about amino acid 430; a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 104 to about amino acid 108; N-myristoylation sites from about amino acid 11 to about amino acid 17, from about amino acid 18 to about amino acid 24, from about amino acid 84 to about amino acid 90, from about amino acid 92 to about amino acid 98, from about amino acid 137 to about amino acid 143, from about amino acid 138 to about amino acid 144, from about amino acid 238 to about amino acid 244, from about amino acid 253 to about amino acid 259, from about amino acid 278 to about amino acid 284, and from about amino acid 282 to about amino acid 288; an amidation site from about amino acid 102 to about amino acid 106; and a prokaryotic membrane lipoprotein lipid attachment site from about amino acid 6 to about amino acid 17. Clone DNA76531-1701 has been deposited with ATCC on November 17, 1998 and is assigned ATCC deposit no. 203465.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 30 (SEQ ID NO:30), evidenced sequence identity between the PRO1759 amino acid sequence and the following Dayhoff sequences: OPDE_PSEAE, TH11_TRYBB, S67684, RGT2_YEAST, S68362, ATSUGTRPR_1, P_W17836 (Patent application WO9715668-A2), F69587, A48076, and A45611.

EXAMPLE 18

Isolation of cDNA Clones Encoding Human PRO5775

DNA96869-2673 was identified by applying the proprietary signal sequence finding algorithm described in Example 2 above. Use of the above described signal sequence algorithm allowed identification of an EST cluster sequence from the LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, CA, designated herein as CLU86443. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte

Table 7B
 Δ Ct values in lung and colon primary tumor and cell line models

Primary Tumor	PRO1759	PRO5775	PRO7133	PRO7168	PRO5725	PRO202	PRO206	PRO264	PRO313	PRO342	PRO542	PRO773	PRO861	PRO1216
HF-000 631	---	1.97 1.70	---	1.43	---	---	---	---	---	---	---	---	---	---
HF-000 641	---	1.90 1.87	---	---	1.17 1.03	---	---	---	---	---	---	---	---	---
HF-000 643	---	1.13 1.21	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 840	1.11	3.64 3.55	2.11	2.65	1.82 2.20 1.99	---	---	---	---	1.35	---	---	---	---
HF-000 842	---	2.56 2.42 2.12 2.88	---	1.73	---	---	---	---	---	1.13	---	---	---	---
HBL100	---	---	---	---	---	---	---	---	---	---	1.20	---	---	---
MB435s	---	---	---	---	---	---	---	---	---	---	---	---	---	---
T47D	---	---	---	---	---	---	---	---	---	---	---	---	---	---
MB468	---	---	---	---	---	---	---	---	---	---	---	---	---	---
MB175	---	---	---	---	---	---	---	---	---	---	---	---	---	---
MB361	---	---	---	---	---	---	---	---	---	---	---	---	---	---
BT20	---	---	---	---	---	---	---	---	---	---	---	---	---	---
MCF7	---	---	---	---	---	---	---	---	---	---	1.14	---	---	---
SKBR3	---	---	---	---	---	---	---	---	---	---	---	---	---	---

Table 7B Continued
 Δ Ct values in lung and colon primary tumor and cell line models

Primary Tumor	PRO1759	PRO5775	PRO7133	PRO7168	PRO5725	PRO202	PRO206	PRO264	PRO313	PRO342	PRO542	PRO773	PRO861	PRO1216
SW480	---	---	---	---	---	---	---	---	---	---	1.35	---	---	---
SW620	---	---	---	---	---	---	---	---	1.03	2.09	1.17 1.13	---	---	---
Colo320	---	---	---	---	---	---	---	---	---	---	---	1.31	---	---
HT29	---	---	---	---	---	---	---	---	---	---	3.08 2.59 3.24 2.68 2.77	1.97	---	---
HM7	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Widr	---	---	---	---	---	---	---	---	---	---	3.35 3.15 2.59 2.94 3.03 2.99	---	---	2.42
HCT116	---	---	---	---	---	---	---	---	---	---	2.09 2.01 2.12 1.87 1.98 2.07	---	---	1.71

Table 7B Continued
 Δ Ct values in lung and colon primary tumor and cell line models

Primary Tumor	PRO1759	PRO5775	PRO7133	PRO7168	PRO5725	PRO202	PRO206	PRO264	PRO313	PRO342	PRO542	PRO773	PRO861	PRO1216
SKCO1	---	---	---	---	---	---	---	---	---	---	1.71	---	---	---
											2.00			
											1.97			
											1.64			
											1.82			
SW403	---	---	---	---	---	---	---	---	---	---	1.73	---	---	1.14
											1.15			
											1.64			
											1.17			
											1.51			
LS174T	---	---	---	---	---	---	---	---	---	1.13	1.41	---	---	1.16

Colo205	---	---	---	---	---	---	---	---	---	---	---	1.41	---	---
HCT15	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HCC 2998	---	---	---	---	---	---	---	---	---	---	---	---	---	---
KM12	---	---	---	---	---	---	---	---	---	---	---	---	---	---
A549	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Calu-1	---	---	---	---	---	---	---	---	---	1.21	---	---	---	---
Calu-6	---	---	---	---	---	---	---	---	---	---	---	---	---	---
H157	---	---	---	---	---	---	---	---	---	---	---	---	---	---
H441	---	---	---	---	---	---	---	---	---	1.65	1.15	1.51	1.71	---

Table 7B Continued
 Δ Cl values in lung and colon primary tumor and cell line models

Primary Tumor	PRO1759	PRO5775	PRO7133	PRO7168	PRO5725	PRO302	PRO206	PRO264	PRO313	PRO342	PRO542	PRO773	PRO861	PRO1216
H460	---	---	---	---	---	---	---	---	---	---	---	---	---	---
SKMES1	---	---	---	---	---	---	---	---	---	---	---	---	---	---
SW900	---	---	---	---	---	---	---	---	---	---	---	---	1.02	---
H522	---	---	---	---	---	---	---	---	---	---	---	---	---	---
H810	---	---	---	---	---	---	---	---	---	---	---	---	---	---
SRCC 1094	---	---	---	---	---	---	---	---	---	---	---	---	---	---
SRCC 1095	---	---	---	---	---	---	---	---	---	---	---	---	---	---
SRCC 1096	---	---	---	---	---	---	---	---	---	---	---	---	---	---
SRCC 1097	---	---	---	---	---	---	---	---	---	---	---	---	---	---
SRCC 1098	---	---	---	---	---	---	---	---	---	---	---	---	---	---
SRCC 1099	---	---	---	---	---	---	---	---	---	---	---	---	---	---
SRCC 1100	---	---	---	---	---	---	---	---	---	---	---	---	---	---
SRCC 1101	---	---	---	---	---	---	---	---	---	---	---	---	---	---

Table 7B Continued
 Δ Ct values in lung and colon primary tumor and cell line models

Primary Tumor	PRO1759	PRO5775	PRO7133	PRO7168	PRO5725	PRO202	PRO206	PRO264	PRO313	PRO342	PRO542	PRO773	PRO861	PRO1216
HF-000 545	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 499	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 539	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 575	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 698	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 756	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 762	---	2.01 1.04	---	---	1.26 1.04	---	---	---	---	---	---	---	---	---
HF-000 789	---	1.30 1.12	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 795	1.32	---	1.08	---	1.02 1.28 1.10	---	---	---	---	---	---	---	---	---
HF-000 811	---	1.82 1.80	1.09	---	---	---	---	---	---	---	---	---	---	---

Table 7B Continued
 Δ Ct values in lung and colon primary tumor and cell line models

Primary Tumor	PRO1759	PRO5775	PRO7133	PRO7168	PRO5725	PRO202	PRO206	PRO264	PRO313	PRO342	PRO542	PRO773	PRO861	PRO1216
HF-000 755	---	---	---	---	---	---	---	---	---	---	---	---	---	---
CT2	---	---	---	---	---	---	1.21	---	1.75	3.04	---	---	2.40 2.35	---
CT3	---	---	---	---	---	---	---	---	---	1.21	---	---	1.52 1.39	---
CT8	---	---	---	---	---	---	---	---	---	1.21	---	---	1.55	---
CT10	---	---	---	---	---	---	1.06	---	---	1.81	1.13	---	1.97 1.33	---
CT12	---	---	---	---	---	---	1.06	---	---	1.41	1.08 1.17	---	1.36	1.18
CT14	---	---	---	---	---	---	1.29	---	---	1.61	1.41	---	1.75 1.17	---
CT15	---	---	---	---	---	---	1.32	---	---	1.41	---	1.04	1.75	---
CT16	---	---	---	---	---	---	1.59	---	---	1.39	---	1.37	1.11	---
CT17	---	---	---	---	---	---	---	---	---	1.19	---	1.34	1.11	---
CT1	---	---	---	---	---	---	---	---	1.28	1.61	---	---	1.09 1.22	---
CT4	---	---	---	---	---	---	---	---	1.57	1.58	---	---	1.16	---
CT5	---	---	---	---	---	---	1.23	---	2.01	2.29	1.06	---	1.95	1.21
CT6	---	---	---	---	---	---	---	---	---	1.20	---	---	---	---

Table 7B Continued
 Δ Ct values in lung and colon primary tumor and cell line models

Primary Tumor	PRO1759	PRO5775	PRO7133	PRO7168	PRO5725	PRO202	PRO206	PRO264	PRO313	PRO342	PRO542	PRO773	PRO861	PRO1216
CT7	---	---	---	---	---	---	---	---	---	---	---	---	1.14	---
CT9	---	---	---	---	---	---	---	---	1.56	1.00	1.03	---	1.00	---
CT11	---	---	---	---	---	---	---	---	2.12	2.27	---	---	1.88	---
CT18	---	---	---	---	---	---	1.33	---	---	---	---	---	---	---
CT25	---	---	---	---	---	---	---	---	---	---	---	---	---	---
CT28	---	---	---	---	---	---	---	---	---	---	---	---	---	---
CT35	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 611	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 613	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-00 1291	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-00 1293	---	2.12 2.09	---	---	---	---	---	---	---	---	---	---	---	---
HF-00 1294	---	2.15 1.99	---	---	---	---	---	---	---	1.57	---	---	---	---
HF-00 1295	---	1.99 2.15	---	---	1.10	---	---	---	---	---	---	---	---	---
HF-00 1296	1.51	4.62 4.78	1.71	---	1.22	---	---	---	---	3.15	---	---	---	---

Table 7B Continued
 ACt values in lung and colon primary tumor and cell line models

Primary Tumor	PRO1759	PRO5775	PRO7133	PRO7168	PRO5725	PRO202	PRO206	PRO264	PRO313	PRO342	PRO542	PRO773	PRO861	PRO1216
HF-00 1297	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-00 1299	---	1.92 1.95	---	---	---	---	---	---	---	---	---	---	---	---
HF-00 1300	---	---	---	---	---	---	---	---	---	---	---	---	---	---
LT7	---	---	---	---	---	1.50 1.79	---	---	---	1.25	1.11	---	---	1.15
LT27	---	---	---	---	---	---	---	---	---	---	---	---	---	---
LT13	---	---	---	---	---	1.64	---	---	---	1.34 2.85 2.12	1.38	2.98	1.33	---
LT1	---	---	---	---	---	1.29 1.15	---	---	---	---	---	---	---	---
LT2	---	---	---	---	---	---	---	---	---	---	---	---	---	---
LT3	---	---	---	---	---	1.67 1.66	---	1.82	---	1.89 1.71	---	---	---	---
LT4	---	---	---	---	---	1.21	---	1.43	---	---	---	---	---	---
LT9	---	---	---	---	---	1.30	---	1.13	1.19	1.51	---	---	---	---
LT12	---	---	---	---	---	1.73	---	---	1.03	2.02 1.74	1.31 1.41	---	1.18 1.38	1.02
LT22	---	---	---	---	---	---	---	---	---	---	---	---	---	---

Table 7B Continued
 ΔCt values in lung and colon primary tumor and cell line models

Primary Tumor	PRO1759	PRO5775	PRO7133	PRO7168	PRO5725	PRO202	PRO206	PRO264	PRO313	PRO342	PRO542	PRO773	PRO861	PRO1216
LT30	---	---	---	---	---	---	---	---	---	---	---	---	---	---
LT33	---	---	---	---	---	---	---	---	---	---	---	---	---	---
LT8	---	---	---	---	---	---	---	---	---	---	---	---	1.00	---
LT21	---	---	---	---	---	---	---	---	---	1.00	1.19	---	---	---
LT1a	---	---	---	---	---	1.26 1.24	---	1.28	---	1.72 1.29	---	---	1.19	---
LT6	---	---	---	---	---	1.75 1.34	---	1.62	---	2.01	---	---	---	---
LT10	---	---	---	---	---	---	---	---	---	2.02 1.06	2.79	---	---	---
LT11	---	---	---	---	---	1.31	---	---	---	1.08 1.88 1.93	---	---	1.03	---
LT15	---	---	---	---	---	1.63	---	---	---	2.12 3.16 2.80	---	---	1.28	---
LT16	---	---	---	---	---	1.30	---	---	2.48	1.05	1.32	2.19	1.33	---
LT17	---	---	---	---	---	1.74	---	1.72	---	1.12 2.26 1.77	1.00 1.45	---	---	---
LT18	---	---	---	---	---	---	---	---	---	---	1.21	---	---	---

Table 7B Continued
 Δ Ct values in lung and colon primary tumor and cell line models

Primary Tumor	PRO1759	PRO5775	PRO7133	PRO7168	PRO5725	PRO202	PRO206	PRO264	PRO313	PRO342	PRO542	PRO773	PRO861	PRO1216
LT19	---	---	---	---	---	1.98	---	---	2.10	3.47 3.02	1.35	---	---	---
LT26	---	---	---	---	---	---	---	---	---	---	---	---	---	---
LT28	---	---	---	---	---	---	---	---	---	---	---	---	---	---
LT29	---	---	---	---	---	---	---	---	---	---	---	---	---	---
LT31	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 854	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 855	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 856	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 831	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 832	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 550	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 551	---	---	---	---	---	---	---	---	---	---	---	---	---	---
HF-000 733	---	---	---	---	---	---	---	---	---	---	---	---	---	---

Table 7B Continued
 Δ Ct values in lung and colon primary tumor and cell line models

Primary Tumor	PRO1759	PRO5775	PRO7133	PRO7168	PRO5725	PRO202	PRO206	PRO264	PRO313	PRO342	PRO542	PRO773	PRO861	PRO1216
HF-000 716	---	---	---	---	---	---	---	---	---	---	---	---	---	---

HCT116, SKCO1, and LS174T.

Because amplification of DNA58801-1052 occurs in various tumors, it is highly probable to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA58801-1052 (PRO779) would be expected to have utility in cancer therapy.

5 PRO1185 (DNA62881-1515):

The ΔC_t values for DNA62881-1515 in a variety of tumors are reported in Table 7A. A ΔC_t of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. Table 7A indicates that significant amplification of nucleic acid DNA62881-1515 encoding PRO1185 occurred: (1) in primary lung tumors: LT3, LT30 and LT26; and (2) in primary colon tumor CT2.

10 Because amplification of DNA62881-1515 occurs in various tumors, it is highly probable to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA62881-1515 (PRO1185) would be expected to have utility in cancer therapy.

PRO1245 (DNA64884-1527):

15 The ΔC_t values for DNA64884-1527 in a variety of tumors are reported in Table 7A. A ΔC_t of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. Table 7A indicates that significant amplification of nucleic acid DNA64884-1527 encoding PRO1245 occurred: (1) in primary lung tumors: LT13, LT15 and LT16; (2) in lung tumor cell line H522; and (3) in primary colon tumor CT15.

20 Because amplification of DNA64884-1527 occurs in various tumors, it is highly probable to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA64884-1527 (PRO1245) would be expected to have utility in cancer therapy.

PRO1759 (DNA76531-1701):

25 The ΔC_t values for DNA76531-1701 in a variety of tumors are reported in Table 7B. A ΔC_t of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. Table 7B indicates that significant amplification of nucleic acid DNA76531-1701 encoding PRO1759 occurred: (1) in primary lung tumors: HF-000840 and HF-001296; and (2) in primary colon tumor center HF-000795.

Because amplification of DNA76531-1701 occurs in various tumors, it is highly probable to play a significant role in tumor formation or growth. As a result, antagonists (*e.g.*, antibodies) directed against the protein encoded by DNA76531-1701 (PRO1759) would be expected to have utility in cancer therapy.

30 PRO5775 (DNA96869-2673):

The ΔC_t values for DNA96869-2673 in a variety of tumors are reported in Table 7B. A ΔC_t of >1 was typically used as the threshold value for amplification scoring, as this represents a doubling of gene copy. Table 7B indicates that significant amplification of nucleic acid DNA96869-2673 encoding PRO5775 occurred: (1) in primary lung tumors: HF-000631, HF-000641, HF-000643, HF-000840, HF-000842, HF-001293, HF-001294, HF-